UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/499,765	02/08/00	HAYASHI Y	46910-DIV2

HM22/0706

DAVID G CONLIN ESQ
DIKE BRONSTEIN ROBERTS & CUSHMAN
130 WATER STREET
BOSTON MA 02109

EXAMINER	
NOLAN, P	
ART UNIT	**PAPER NUMBER**
1644	4

DATE MAILED: 07/06/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/499,765	Hayashi et al.
Examiner	Group Art Unit
Nolan	1644

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

P riod for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☐ Responsive to communication(s) filed on _____.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

Dispositi n f Claims

☒ Claim(s) 14-19 is/are pending in the application.

Of the above claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 14-19 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claim(s) _____ are subject to restriction or election requirement.

Applicati n Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Pri rity und r 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

Attachment(s)

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 3

☐ Interview Summary, PTO-413

☒ Notice of Reference(s) Cited, PTO-892

☐ Notice of Informal Patent Application, PTO-152

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☒ Other SEQ TRANSFER LETTER

Office Action Summary

Part III DETAILED ACTION

1. This application is a divisional of 09/076,938 which is divisional of 08/736,434.

2. The specification on page 1 should be amended to reflect the status of the parent application, serial number 09/076,938.

3. Claims 14-19 are pending.

4. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Applicant is requested to transfer the CRF from either parent Application into the present Application according the enclosed request form.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

6. Claims 14-19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant has not disclosed how to use the claimed invention to treat patients suffering from any autoimmune disease or specifically Sjogren's disease with alpha-fodrin or fragments or muteins thereof. There is insufficient evidence of the invention with respect to the human in vivo operability of the claimed peptides or analogs thereof to use the applicant's invention.

Pharmaceutical therapies are unpredictable for the following reasons; (1) the protein may be inactivated before producing an effect, i.e. such as proteolytic degradation, immunological inactivation or due to an inherently short half life of the protein; (2) the protein may otherwise not reach the target area because, for example, (a) the protein may not be able to cross the mucosa, (b) the protein may be adsorbed or absorbed by fluids, cells and tissues where the protein has no effect; and (3) other functional properties, known or unknown, may make the protein unsuitable for in vivo use, i.e. may produce adverse side effects prohibitive to the use of such treatment. See MPEP 608.01(p).

Fox (U), teaches that Sjogren's disease has a pathology that is mediated autoreactive T cells (page 440, in particular). The goal of peptide immunotherapy of T-cell-mediated autoimmunity is to induce anergy in self reactive T cells. However Wraith et al., (V, Cell 59: 247-255, 1989) teach the "Inhibition of the response restricted by one class II molecule may lead only to the escape to an autoimmune response to a separate epitope restricted by a different class II molecule." (page 253 column 1, in particular). Applicant has provided only limited murine in vivo experiments to demonstrate operability of the alpha-fodrin specific peptide. Since human and mice display different MHC haplotypes and applicant has given no guidance as to how their peptide specific therapy would overcome autoreactive T cell escape mechanisms in humans it would require and undue amount of experimentation to one of skill in the art to practice the claimed invention and this is not sanctioned by the statute.

Furthermore, Tisch et al., (W, P.N.A.S. 91:437-438) teach that treating an ongoing T-cell-mediated autoimmunity by administering an antigen peptide may have an immunizing effect and exacerbate the disease condition (page 437, column 3, in particular). Since applicant has not provided any working examples of the efficacy of the alpha-fodrin muteins or fragments in treating already established Sjogrens disease patients, it would require and undue amount of experimentation to one of skill in the art to practice the claimed invention and this is not sanctioned by the statute.

Lastly, besides the specific polypeptide fragment of alpha-fodrin disclosed in the specification, the specification fails to provide any guidance as to how to determine the active amino acid residues within the scope of the claimed invention. These claims are drawn to any polypeptides which are comprised of alpha-fodrin or a fragment or mutein thereof. There is no predictability in the isolation of polypeptides which fulfill the requirements of the claims because it is difficult to predict the 3-D structure of modified polypeptides and the resulting therapeutic capabilities of such peptides for treating patients is limited by such factors as steric hinderance and predictability of the mutagenesis method. As applicant well knows, the predictability of changes to an amino acid sequence is practically nil as far as activities are concerned. In re Fisher, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary

in order to satisfy the statute.

In view of the lack of predictability of the art to which the invention pertains and the lack of established clinical protocols for effective autoimmune therapies; undue experimentation would be required to practice the claimed methods with a reasonable expectation of success.

7. Claim 17 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 17 has an amino acid sequence but no SEQ ID NO. Correction is required.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick Nolan whose telephone number is (703) 305-1987. The examiner can normally be reached on Monday through Friday from 8:30 am to 4:30 pm.

9. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Christina Chan, can be reached at (703) 305-3973. The FAX number for our group, 1644, is (703) 305-7939. Any inquiry of a general nature relating to the status of this application or proceeding should be directed to the Group receptionist, whose telephone number is (703) 308-0196.

Patrick J. Nolan

Patrick J. Nolan, Ph.D.
Patent Examiner, Group 1640
June 29, 2000